Testimony
Before the Special Committee on Aging
United States Senate

Human Longevity and Aging Research

Statement of

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Mr. Chairman, Senator Breaux, and Members of the Committee:

Thank you for inviting me to appear before you today to discuss human longevity and innovations in the field of aging research. I am Dr. Richard Hodes, Director of the National Institute on Aging (NIA), and I am delighted to be here today to discuss this important topic.

Life Expectancy

Today, more people than ever before are enjoying robust health and productivity well into their seventies, eighties, and beyond.[1] Life expectancy for Americans, around 49 years in 1900, has increased over the past century to about 76, thanks to improvements in health care, nutrition, and the overall standard of living for most people. Furthermore, demographic projections suggest that life expectancy for men and women who maintain the healthiest lifestyle patterns will continue to increase. In fact, centenarians (persons 100 years of age and older) are the fastest-growing segment of our population.

As importantly, Americans are not only living longer, but also remaining healthier and more active well into older age. A recent meta-analysis of demographic studies confirms that disability among America's elders has declined steadily over the past decade.

More older Americans are able to participate in "instrumental activities of daily living," such as performing household chores and managing their own medications, while fewer are experiencing limitations in basic physical tasks such as walking or climbing

[1] Federal Interagency Forum on Aging Related Statistics. *Older Americans 2000: Key Indicators of Well-Being.* 2000.

stairs. The prevalence of severe cognitive impairment also appears to be declining, although this finding needs verification by additional study.

At the same time, diseases of aging continue to affect many older men and women, seriously compromising the quality of their lives. For example, more than half of all Americans over age 65 show evidence of osteoarthritis in at least one joint.[2] Over half of Americans over age 50 have osteoporosis or low bone mass[3]. Cardiovascular disease, cancer, and diabetes remain common among older Americans. And, according to the Alzheimer's Association, as many as 4 million Americans suffer from Alzheimer's disease (AD), the most common cause of dementia among older persons.

At the NIA and other Institutes and Centers at the National Institutes of Health (NIH), we are working to understand factors that affect human longevity and ways to improve quality of life. We know that to prolong life we must improve diagnostic methods to ensure early and reliable detection of disease and pathology; we must encourage individuals to make healthy lifestyle choices; and we must develop effective interventions for disease and disability.

We anticipate that our efforts to reach these goals will be influenced by findings from a number of emerging technological fields, including medical imaging, computational biology, proteomics, regenerative medicine, and even nanotechnology. The NIH is currently supporting research in all of these areas in the context of the NIH Roadmap initiative to enhance research infrastructure and methodology.

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[2] See "Handout on Health: Osteoarthritis," National Institute of Arthritis and Musculoskeletal and Skin Diseases, July 2002

[3] See America's Bone Health: The State of Osteoporosis and Low Bone Mass in Our Nation. National Osteoporosis Foundation, February 2002.

Longevity Research

An intriguing area of investigation is the analysis of genetic contributions to longevity. **(Chart #1)** Research findings indicate that similar mechanisms and pathways regulate longevity in diverse species, including yeast, fruit flies, nematodes, and mice, and that equivalent mechanisms and pathways may exist in humans. In 1993, NIA-supported researchers formed the Longevity Associated Gene (LAG) Initiative in order to identify genes and processes involved in longevity regulation across species. The ultimate goal of the LAG initiative is to relate findings in other species to the regulation of human biology, contributing to identification of age-related changes in physiological systems. Other studies, including the NIA-supported New England Centenarian Study, are identifying genetic and other factors that contribute to successful human aging. In the Centenarian Study, data on 444 centenarian families and over 2,000 siblings will provide information on factors that support extreme longevity and will suggest directions for future research.[4] **(Chart #2)**

In addition to studies of possible genetic influences on longevity, NIA supports and conducts extensive research on diseases and conditions that often shorten life, or that seriously compromise the quality of life of older Americans.

Two conditions that illustrate the ways in which advances in technology are leading to new findings that may both extend life and improve overall quality of life are Alzheimer's disease (AD) and obesity.

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[4] Perls, T.T., et al. Life-long sustained mortality advantage of siblings of centenarians. *Proceedings of the National Academy of Sciences. 2002* ;**99**(12**)**, 8442-7.

Alzheimer's Disease

AD is a devastating condition with a profound impact on individuals, families, the health care system, and society as a whole. According to data from the Alzheimer's Association, approximately 4 million Americans are currently battling AD. Moreover, the rapid aging of the American population threatens to increase this burden significantly in the coming decades: Demographic studies suggest that if current trends hold, the annual number of incident cases of AD will begin a sharp increase around the year 2030, when all the baby boomers (born between 1946 and 1964) will be over age 65. By the year 2050, the number of Americans with AD could double.[5]

We have made, and are continuing to make, considerable progress in our ability to diagnose, treat, and even prevent AD, and advances in imaging technology have played an important role in each of these areas. The development and refinement of powerful imaging techniques that target anatomical, molecular, and functional processes in the brain is giving us an improved ability to identify people who are at very high risk for AD, as well as a greater understanding of the disease's pathology. For example, recent studies suggest that positron emission tomography (PET) scanning of metabolic changes in the brain and magnetic resonance imaging (MRI) scanning of structural brain changes may be useful tools for predicting future decline associated with AD and other neurodegenerative diseases.

Several new findings in mouse models illustrate the promise of advances in imaging technology. In one study, researchers found that changes in brain structure can be

[5] Hebert LE, Beckett LA, Scherr PA, and Evans DA. Annual Incidence of Alzheimer Disease in the United States Projected to the Years 2000 Through 2050. Alzheimer Dis. Assoc. Disord. 15: 169-173, 2001.

detected by magnetic resonance microscopy before AD's characteristic amyloid plaques appear in the brain, suggesting that subtle pathologic changes are occurring long before signs and symptoms of the disease appear. In another study, investigators imaging the brains of mice bearing AD-like pathology were able to directly observe the clearance of amyloid deposits after the mice were treated using an immune approach **(Chart #3)**; similar techniques in humans may ultimately enable the in vivo evaluation of preventive or therapeutic interventions against AD. Investigators in a third study, the results of which will soon be published, have created a new mouse model that carries a "reporter gene" – a gene that signals the occurrence of a particular event – in the brain. The gene itself emits light in response to certain types of injury to brain cells, and with an ultrasensitive camera – similar to the ones used in astronomy to detect low levels of light from faraway stars – we can capture and quantify light generated within the mouse (**Chart #4)**. This technology will facilitate new approaches to the study of key processes in living mice, and to correlating gene expression with disease outcome. Because each mouse can be imaged repeatedly, disease progression and responses to therapeutic intervention can be assessed. Other emerging technologies hold great promise in developing therapeutic approaches to AD, for example by blocking plaque and tangle formation, by stimulating repair of brain tissue, or by delivery of time-released medication.

Obesity

Recent research findings have further demonstrated the significant link between chronic obesity and heart disease, adult-onset diabetes, and certain cancers. These conditions ultimately shorten lifespan and decrease quality of life. Prevention and early

treatment of obesity will undoubtedly contribute to improvements in longevity and functional ability.

In a recent NIH co-funded study, a novel technique known as RNA interference (RNAi), in which double-stranded RNA is inserted into a cell to inhibit the activity of one or more genes, was used to identify genes involved in the regulation of fat metabolism in roundworms. **(Chart #5)** Using this new approach, each of the 17,000 genes of the roundworm was inactivated or "turned off." Researchers found that the inhibition of 305 genes decreased body fat, whereas the inhibition of 112 genes increased fat storage. This finding could lead to the identification of new targets for treatment of obesity and its associated diseases.

Closing Remarks

At the turn of the last century, it would have been difficult to imagine the strides medical research has made on longevity. It is our hope that with our increasing knowledge in the field of aging that we can help individuals to not only live longer, but to maintain functional and productive lives. I would like to thank the Committee and Congress for your support of NIH and NIA and for holding today's hearing on this crucial issue, the future of human longevity.